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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/560,119 | 05/17/2006 | David Alan Owen | CELL-0311 | 2779 |
| 20306 | 7590 | 10/15/2008 | EXAMINER | |
| MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP | | | LEESER, ERICH A | |
| 300 S. WACKER DRIVE | | | | |
| 32ND FLOOR | | | ART UNIT | PAPER NUMBER |
| CHICAGO, IL 60606 | | | 1624 | |
| | | | | |
| | | | MAIL DATE | DELIVERY MODE |
| | | | 10/15/2008 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/560,119 | OWEN ET AL. | |
| | Examiner | Art Unit | |
| | Erich A. Leeser | 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on ____.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-19 is/are pending in the application.
 - 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) Claim(s) ____ is/are allowed.
- 6) Claim(s) 1-19 is/are rejected.
- 7) Claim(s) ____ is/are objected to.
- 8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on ____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. ____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9-25-06</u> . | 6) <input type="checkbox"/> Other: ____ . |

DETAILED ACTION

Claims 1-19 are currently pending in this application.

Priority

Acknowledgement is made that this application is a 371 of PCT/GB04/02638, filed on June 18, 2004 and which claims the benefit of foreign priority to UK 0314244.5, filed on June 19, 2003 and also claims the benefit of foreign priority to UK 0325834.0, filed on November 5, 2003.

Information Disclosure Statement

The references cited in the IDS, dated November 6, 2006, are made of record.

Claim Rejections – 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for making solvates of the claimed invention. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

The nature of the invention:

The invention is drawn to a compound of formula (1) ... “or a salt, solvate, hydrate, tautomer, isomer or N-oxide thereof.” The specification is not adequately enabled to show how to make solvates of the compounds of formula (1).

The compounds of formula (1) embrace hydroxamate sulfonamides as cd23 shedding inhibitors with their core substituted with variable groups Cy, m, n, and various R groups.

Even a cursory calculation of the number of compounds embraced in the instant formula (1) would result in at least thousands of compounds. This is of course far more compounds than the specification enables one skilled in the art to make. Thus, the genus embraced in claim 1 is too large and there is no teaching of any solvate of this large genus.

The state of the prior art:

A search in the pertinent art, including water as solvent resulted in a pertinent reference, is indicative of the unpredictability of solvate formation in general. The state of the art is that it is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of an organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph of West, Anthony R., *Solid State Chemistry and Its Applications*, Wiley, New York, 1988, 358. The solvent molecule is a species introduced into

the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph: “it is not usually possible to predict whether solid solutions will form, or if they do form what is the compositional extent”. West, Anthony R., *Solid State Chemistry and Its Applications*, Wiley, New York, 1988, 365. Thus, in the absence of undue experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent is added per molecule of host.

The predictability or lack thereof in the art:

For the reasons stated *supra*, the solvates as applied to the above-mentioned compounds claimed by the Applicant are not art-recognized compounds and hence there should be an enabling disclosure in the specification with working example(s).

The amount of direction or guidance present:

Examples illustrated in the experimental section are limited to making the compounds not related to solvates. There is no example of solvates of the instant compounds. A multiplicity of compounds were shown in the examples of the specification each of which come in contact with a solvent but there is no showing that the instant compounds formed solvates. Hence it is clear that merely bringing the compounds in contact with solvent does not result in solvate and additional direction or guidance is needed on how to make them. The specification has no such direction or guidance.

The presence or absence of working examples:

There is no working example of any solvate formed. These cannot be simply willed into existence. “The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there, is no evidence that such

compounds exist... the examples of the '881 patent do not produce the postulated compounds...

there is ... 'no evidence that such compounds even exist.' *Morton Int'l Inc. v. Cardinal Chem.*

Co., 5 F.3d 1464, 28 USPQ2d 1190 (1993). The same circumstance appears to be true here.

There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, there should be a showing of supporting evidence that solvates of these compounds exist and therefore can be made.

The breadth of the claims:

The breadth of the claims include all of the thousands of compounds of formula (1) of claim 1 as well as the presently unknown list of potential solvate derivatives embraced by this term. This term is important in claim 1 because claims are to be given their broadest reasonable interpretation that is consistent with the specification. Because the specification does not adequately teach one skilled in the chemical arts how to sufficiently make the claimed solvates of the present invention without undue experimentation, the scope of the claims is broader than the scope of the specification. It would not be obvious to one skilled in the art how to make the solvates of the present invention. Therefore, the scope of enablement provided to one skilled in the art by the disclosure is not commensurate with the scope of protection sought by the claims.

The quantity of experimentation needed

The specification has no support, as noted *supra*, for the desired solvates of the compounds of formula (1). As noted above, the genus embraces at least thousands of compounds and hence the breadth of the claims is broad. The quantity of experimentation needed would be an undue burden on one skilled in the chemical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated *supra*. Even with the undue

burden of experimentation, there is no guarantee that one would get the product of desired solvates of the compounds of formula (1) embraced in the instant claims.

In view of the seven factors, *supra*, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Claim Rejections 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

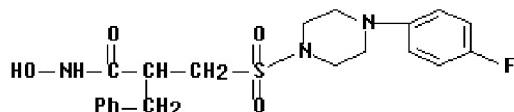
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-16 and 19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Barlaam, et al., U.S. Patent Pub. No. 2003/139419.

Art Unit: 1624

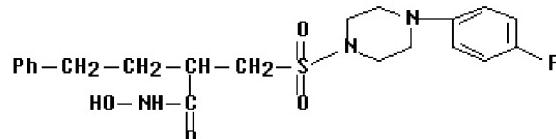
Barlaam, et al., teaches arylpiperazines as metalloproteinase inhibitors. Generically, claim 1 of the reference renders the scope of instant claim 1 obvious. For example, the following compounds of the reference render instant claim 1 obvious:

[[[4-(4-fluorophenyl)-1-piperazinyl]sulfonyl]methyl]-N-hydroxy-benzenepropanamide,



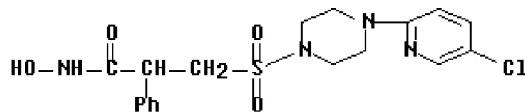
when Cy is phenyl, R³ is hydrogen, R⁴ is F, m and n are both 1, R^a, R^b, and R² are all hydrogen and R¹ is C₁alkylaryl;

[[[4-(4-fluorophenyl)-1-piperazinyl]sulfonyl]methyl]-N-hydroxy-benzenebutanamide,



when Cy is phenyl, R³ is hydrogen, R⁴ is F, m and n are both 1, R^a, R^b, and R² are all hydrogen and R¹ is C₂alkylaryl;

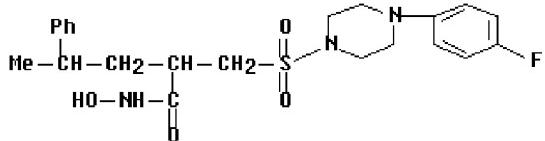
[[[4-(5-chloro-2-pyridinyl)-1-piperazinyl]sulfonyl]methyl]-N-hydroxy-benzeneacetamide,



when Cy is heteroaryl, R³ is hydrogen, R⁴ is Cl, m and n are both 1, R^a, R^b, and R² are all hydrogen and R¹ is aryl;

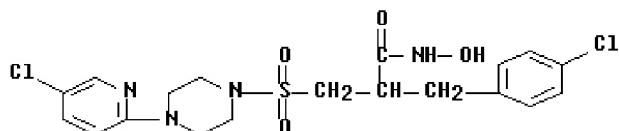
Art Unit: 1624

[[[4-(4-fluorophenyl)-1-piperazinyl]sulfonyl]methyl]-N-hydroxy-g-methylbenzenebutanamide,



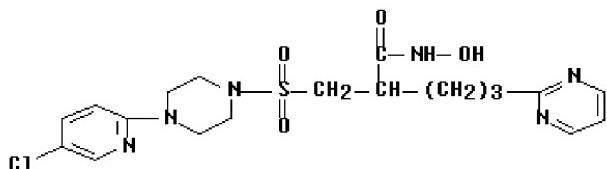
when Cy is phenyl, R³ is hydrogen, R⁴ is F, m and n are both 1, R^a, R^b, and R² are all hydrogen and R¹ is C₃alkylaryl;

4-chloro-a-[[[4-(5-chloro-2-pyridinyl)-1-piperazinyl]sulfonyl]methyl]-N-hydroxybenzenepropanamide,



when Cy is heteroaryl, R³ is hydrogen, R⁴ is Cl, m and n are both 1, R^a, R^b, and R² are all hydrogen, R⁷ is Cl, and R¹ is C₁alkylaryl;

[[[4-(5-chloro-2-pyridinyl)-1-piperazinyl]sulfonyl]methyl]-N-hydroxy-2-pyrimidinepentanamide,



when Cy is heteroaryl, R³ is hydrogen, R⁴ is Cl, m and n are both 1, R^a, R^b, and R² are all hydrogen, and R¹ is C₃alkylheteroaryl.

In all of these examples, the only difference between this exemplified compound and the generic teaching of instant claim 1 is hydrogen versus methyl on the phenyl. It is well

established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. *In re Wood*, 199 USPQ 137 (CCPA 1978) and *In re Lohr*, 137 USPQ 548, 549 (CCPA 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity.

As such, claims 1-16 and 19 are rendered obvious by Barlaam, et al., U.S. Patent Pub. No. 2003/139419.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you

Art Unit: 1624

would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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